Amendments to the Drawings

Please add new Figures 9A, 9B, and 9C to the Drawings.

Attachments: New Figures 9A, 9B, and 9C (3 sheets)

REMARKS/ARGUMENTS

Claims 1-29 are pending in the above-identified application. Claims 4-7, 10-12, 16 and 24-29 have been withdrawn from consideration as drawn to non-elected inventions. By this amendment, the specification is amended to incorporate the Sequence Listing as well as to incorporate the required sequence identifier ("SEQ ID NO:3") for the antigenic peptide designated PSM-PX. Also, the specification and drawings are amended to explicitly recite subject matter incorporated by reference in the application as filed. Further, claim 2 is canceled without prejudice and claims 3, 18, and 21 are amended for clarity as set forth in detail herein. No new matter is added by these amendments. Applicants respectfully request reconsideration of the application in light of these amendments and the following remarks.

Sequence Listing

The Examiner has objected to the lack of a sequence listing under 37 C.F.R. §§ 1.821 - 1.825. As noted above, the specification has been amended to incorporate the Sequence Listing. The computer readable form of the Sequence Listing is submitted herewith on a diskette and the written form is submitted on paper. The information obtained on the computer readable diskette was prepared through the use of "PatentIn 3.3." The Sequence Listing information recorded on the computer readable diskette is identical to the paper copy of the Sequence Listing submitted herewith. No new matter is added by this submission. In light of the above, withdrawal of the present objection is respectfully requested.

Incorporation by Reference

The Examiner has objected to the specification based on the incorporation by reference of WO 2004/000444. The Examiner contends that this incorporation by reference is "improper because it is apparent that the tangential flow filtration procedure is essential to practice the claimed invention."

As indicated by the Examiner, WO 2004/000444 relates to a tangential flow filtration procedure. Accordingly, Applicants believe the Examiner's statements, regarding this subject matter as "essential" to the invention, pertain only to claims 17 and 18, which specifically recite dendritic cell enrichment by "tangential flow filtration."

Further, Applicants respectfully disagree with the Examiner's view of the material incorporated by reference as being "essential," at least insofar as this subject matter was already available to the public by virtue of International Patent Application Publication WO 2004/000444. "Essential material" is defined by 37 C.F.R. § 1.57(c) as that material necessary to comply with the provisions of 35 U.S.C. § 112 for written description, enablement, and best mode. It is well established that under 35 U.S.C. § 112, first paragraph, a specification need not explicitly disclose, and preferably omits, what is already known and publicly available to the skilled artisan. *See, e.g.*, MPEP § 2164.05(a).

While Applicants disagree with the objection as stated above, but in order to further expedite prosecution of this application, the specification has been amended to directly incorporate disclosure from WO 2004/000444. Support for these amendments is found specifically at page 9, lines 20-26; page 11, lines 16, 17 and 20-23; page 12, line 24 to page 20, line 15; page 22, lines 16-33; and Figures 1A to 1C of WO 2004/000444, which describes, *inter alia*, the tangential flow procedure and its use for enrichment of dendritic cell precursors. A Declaration under 37 C.F.R. § 1.57(f) (*In re Hawkins* declaration) is attached hereto, establishing that no new matter is added by these amendments. In view of these amendments and the remarks above, withdrawal of the present objection is respectfully requested.

Claim Objections

Claims 18 and 21 have been amended for clarity in view of the Examiner's objections. Specifically, claim 18 has been amended to recite the claimed subject matter in the present tense; and claim 21 has been amended to delete the term "is" from the phrase "comprises

is." Applicants note that these amendments merely correct obvious grammatical or typographical errors. Accordingly, no new matter is added by these amendments.

Rejections under 35 U.S.C. §112, second paragraph

Claims 21 and 22 stand rejection under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. The Examiner contends that it is "unclear, and hence indefinite, how a method that requires the 'absence of additional cytokines' can also employ IFN-γ." Applicants traverse the instant rejection.

A claim is definite where one of skill in the art would understand the scope of the claim when the claim is read in light of the specification. *See North Am. Vaccine, Inc. v. American Cyanamid Co.*, 28 USPQ2d 1333, 1339 (Fed. Cir. 1993). Here, claim 1, from which claims 21 and 22 depend, recites a method for "differentiating monocytic dendritic cell precursors" into immature dendritic cells. As described and shown in the specification, the differentiation of monocytic dendritic cell precursors is achieved using GM-CSF in the absence of other cytokines, as claimed. (*See* specification at, *e.g.*, paragraphs [0039] and [0040] and Example 1.) The specification further discusses the maturation of immature dendritic cells into mature dendritic cells by, for example, contacting the immature dendritic cells that ***have been*** cultured in the presence of GM-CSF alone with effective amounts or concentrations of a dendritic cell maturation agent," (*e.g.*, IFNγ). (*Id.* at ¶ [0042] (emphasis provided).) Consistent with this disclosure, claim 20, from which claims 21 and 22 depend, recites "further contacting the ***differentiated*** dendritic cell precursors with a dendritic cell maturation agent." (Claim 20 (emphasis provided).) Thus, claims 21 and 22 require that the dendritic cell precursors, contacted with IFNγ, should already be differentiated into immature dendritic cells according to the steps recited in claim 1.

In view of the above, it would be clear to the skilled artisan, reading the claims in light of the specification, that the step of inducing maturation of differentiated dendritic cell precursors is carried out subsequent to the differentiation of the dendritic cell precursors into

immature dendritic cells. For this reason, there is nothing inconsistent with the use of IFNγ as a maturation agent, since obtaining immature dendritic cells can first be carried out using GM-CSF in the absence of other cytokines, as recited in claim 1, and then followed with contacting the immature dendritic cells with IFNγ, as recited in claims 21 and 22.

For at least the reasons set forth above, claims 21 and 22 are not indefinite under 35 U.S.C. § 112, second paragraph. Withdrawal of the present rejection is respectfully requested.

Rejections under 35 U.S.C. §112, first paragraph

Claims 20 and 21 stand rejected as allegedly failing to comply with the enablement requirement under 35 U.S.C. § 112, first paragraph. The Examiner contends that the specification "provides insufficient data to enable claims drawn to the method as claimed." Essentially, the Examiner's position appears to be that there is an alleged inconsistency between claim 1, which recites a method for "differentiating monocytic dendritic cell precursors into immature dendritic cells," and claims 20 and 21 (depending from claim 1), which specify contacting the differentiated precursors with a maturation agent, such as, *e.g.*, BCG and IFN-γ. The Examiner states that "it is evident to one of ordinary skill in the art that a method that involves contacting differentiated precursors with the maturation agents BCG and IFN-γ would result in a mature dendritic cell, and not an immature dendritic cell, as claimed." Applicants traverse the instant rejection.

For reasons substantially as set forth above in response to the rejection under 35 U.S.C. § 112, second paragraph, there is nothing inconsistent with the use of a maturation agent such as IFNγ or BCG, since obtaining immature dendritic cells can first be carried out using GM-CSF in the absence of other cytokines, as recited in claim 1, and then followed with contacting the immature dendritic cells with IFNγ, as recited in claims 20 and 21. Stated another way, it would be clearly evident to the skilled artisan reading the specification that, in obtaining mature dendritic cells from monocytic dendritic cell precursors as described, the precursors are

first differentiated into immature dendritic cells. (*See* specification at, *e.g.*, paragraphs [0039] to [0042].) Thus, in the process of carrying out the method as recited in claims 20 and 21, the method as recited in claim 1 is also carried out, with the resulting immature dendritic cells being used to obtain mature dendritic cells.

Moreover, contrary to the Examiner's assertion, the subject matter of claims 20 and 21 is predictable in light of the specification and knowledge in the art. The specification as filed demonstrates that the differentiation of dendritic cell precursors into immature dendritic cells can be carried out according to claim 1 (*see, e.g.*, Example 1), and further demonstrates that the use of differentiated precursors obtained by a process according to claim 1 can be further contacted with a maturation agent to obtain mature dendritic cells (*see, e.g.*, Example 2). The Examiner also acknowledges that Bosche *et al.* (Abstract C30, *J. Invest. Derm.*, 2001) evidences BCG and IFNγ as potent inducers of DC maturation. Accordingly, no undue experimentation would be required to carry out the method as claimed.

In view of the above, claims 20 and 21 are enabled by the specification under 35 U.S.C. § 112, first paragraph. Withdrawal of the present rejection is respectfully requested.

Rejections under 35 U.S.C. §102(b)

Claims 1-2, 14, 19, and 23 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Sallusto and Lanzavecchia (*J. Exp. Med.* 179:1109-1118, 1994) (hereinafter "Sallusto"). The Examiner states, *inter alia*, that Sallusto teaches a method for generating dendritic cells from peripheral blood mononuclear cells ... by culturing in GM-CSF in the absence of additional cytokines." The Examiner, citing to Table 1, further asserts that Sallusto's "dendritic cells are immature, as evidenced by their expression of CD11c and MHC, but lack of expression of B7." Applicants traverse the instant rejection.

Contrary to the Examiner's assertion, Sallusto's cells, cultured in GM-CSF without IL-4, are not immature dendritic cells. Sallusto states that the "identification of GM-CSF/IL-4-expanded cells as DCs was based on three well-established and accepted criteria,"

which includes, *inter alia*, "their surface phenotype, ***with high expression of CD1***, MHC class I and II, Ii, FcγRII, ***B7***, CD40, ICAM-1, LFA-3, and CD11c." (Sallusto at p. 1115, 1st col., 1st full paragraph (emphasis provided).) An examination of the data from Table 1 of Sallusto clearly shows that cells cultured with GM-CSF only were negative for CD1. Further, Table 1 shows B7 expression as "±" as opposed to "+" (positive) for the immature DCs obtained with GM-CSF + IL-4. Moreover, Sallustro states that "[o]ur DC lines were generated from adult peripheral blood and ***require*** IL-4 in addition to GM-CSF to maintain the immature, antigen presenting competent state." (*Id.* at p. 1114, 2nd col., last paragraph, bridging to p. 1115, 1st col. (emphasis provided).) Accordingly, per the disclosure of the Sallusto reference, Sallusto's cells cultured in the presence of GM-CSF only are not immature DCs.

Applicants note in particular that the Examiner himself has acknowledged the Sallusto as evidencing a "lack of B7" expression in the "GM-CSF only cells." The Examiner, however, incorrectly interprets a "lack of B7" expression as a characteristic of immature dendritic cells. To the contrary, while B7 expression is upregulated in dendritic cells upon maturation, it is well known and accepted in the art that dendritic cells also express B7 in their immature form. This knowledge in the art is evidenced by the Sallusto reference itself, as cited above with respect to surface phenotype. Further, the present specification as filed shows surface expression of B7 molecules (CD80 and CD86) on immature dendritic cells obtained by the methods of the present invention, as shown in, *e.g.*, Examples 3 and 6 and the corresponding Figures 4 and 8, respectively.

In any event, irrespective of B7 expression, as Sallusto's "GM-CSF only" cells also clearly lack expression of the dendritic cell marker CD1, including CD1a (*see* Sallusto at Table 1), it is clear that these cells are not immature DCs. In this respect, and in contrast to Sallusto's "GM-CSF only cells," the immature dendritic cells of the present application were shown to express CD1a in addition to B7. (*See* specification at, *e.g.*, Examples 1, 3, 5, and 6, and corresponding Figures 1, 4, 6A, and 8A, respectively.)

For at least the reasons above, Sallusto does not disclose or suggest the differentiation of monocytic dendritic precursor cells into immature DCs by culturing the

precursors in the presence of GM-CSF in the absence of additional cytokines, as presently claimed. Accordingly, Sallusto does not anticipate the present invention under 35 U.S.C. § 102(b). Withdrawal of the present rejection is respectfully requested.

Rejections under 35 U.S.C. §103(a)

Sallusto in view of Bernard, Bosch, or Lewalle

Claims 3, 8, 9, 13, 15, and 20-22 stand rejected under 35 U.S.C. § 103 as follows:

Claims 3, 8, and 9 over Sallusto in view of Bernard *et al.* (*Hematol. Cell. Ther.* 40:17-26, 1998);

Claims 13 and 20-22 over Sallusto in view of Bosch *et al.* (Abstract C30, *J. Invest. Derm.*, 2001); and

Claim 15 in view of Lewalle *et al.* (*J. Immunol. Methods* 240:69-78, 2000).

Applicants traverse the instant rejection. A *prima facie* case of obviousness requires, *inter alia*, a teaching or suggestion of each and every claim limitation in the cited art. MPEP § 2143.03. Here, for the reasons set forth above in response to the rejection under 35 U.S.C. § 102(b), Sallusto's cells obtained by culturing with GM-CSF in the absence of additional cytokines are not "immature dendritic cells," as recited in the claims. None of the other cited references cure this deficiency, since the cells of both Bernard and Lewalle are cultured in GM-CSF in the presence of IL-4 (*see* Bernard at, *e.g.*, p. 21, 2nd col.; Lewalle at, *e.g.*, p. 70, 2nd col., ¶2.1.2); and Bosch discusses conditions for obtaining mature dendritic cells (*see* Bosch, Abstract). Accordingly, the cited art does not teach or suggest each and every limitation of the present claims.

For at least the reasons above, the present claims are patentable under 35 U.S.C. § 103 over Sallusto, either alone or in any combination with Bernard, Bosch, or Lewalle. Withdrawal of these rejections is therefore respectfully requested.

Sallusto in view of US 2005/0173315

Claims 17 and 18 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Sallusto in view of U.S. Patent Application Publication 2005/0173315 ("the '315 Application").

While Applicants believe the present rejection to be obviated in view of the arguments set forth above in response to the rejection under § 102(b), Applicants further note that the present application was filed before publication of the '315 Application (published August 11, 2005). Therefore, the '315 Application can qualify as prior art only under one or more of subsections (e), (f), and (g) of 35 U.S.C. § 102; and, consequently, patentability of the claimed invention is not precluded by § 103 if the claimed invention and subject matter of the '315 Application were commonly owned or subject to an obligation of assignment to the same person at the time claimed invention was made. *See* 35 U.S.C. § 103(c). Applicants hereby state that the claimed invention and subject matter of the '315 Application were commonly owned at the time the claimed invention was made.

In light of the above, the '315 Application is not available as prior art against the present application under 35 U.S.C. § 103. Withdrawal of the present rejection is respectfully requested.

Other Amendments

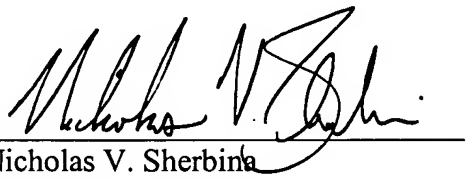
Claim 2, which recites "wherein the monocytic dendritic cell precursors are non-activated," has been canceled to eliminate redundancy in the claims, as claim 1 already specifies "non-activated monocytic dendritic cell precursors." Claim 3 has been amended accordingly to change its dependency from claim 2 to claim 1.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 206-467-9600.

Respectfully submitted,

Date: June 15, 2006 By: 

Nicholas V. Sherbina
Reg. No. 54,443

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 206-467-9600
Fax: 415-576-0300
Attachments
NVS/BWP:jms:mmm
60687924 v1